

### REMARKS

Claims 69, 70, 75, 76 and 80 have been cancelled without prejudice. Claims 70, 71, 77-79, 81, 85 and 87-89 have been amended. Claims 61, 81 and 87-89 were revised to specify that breast cancer is diagnosed. Claims 71 and 85 were revised to further clarify the claims by excising the phrase "evidence of". Claims 77-79 were revised to recite that "altered" levels of the expression product are indicative of breast cancer. Claim 87 was also revised to further clarify the hybridization language. New claims 91-93 have been added and are drawn to the diagnosis of carcinoma.

Applicants have amended the specification at paragraph [0149] to delete reference to a hyperlink.

No new matter has been added.

Applicants respectfully reconsideration and allowance of claims 61, 71, 72, 74, 77-79, 81, 85-89 and 91-93 in view of the above amendments and following remarks.

#### Claim Objections

The Office objected to claim 70 for allegedly failing to further limit the subject matter of the previous claim. Claim 70 has been cancelled, therefore rendering the objection moot.

#### Rejection under 35 U.S.C. §112, first paragraph

The Office rejected claims 61, 69-72, 74-81 and 85-89 under 35 U.S.C. §112, first paragraph as allegedly containing new matter. The Office asserts that although "the specification does disclose carcinoma associated (CA) nucleic acids can be up-regulated, as well as down regulated in carcinomas, however there seems to be insufficient contemplation for the up-regulation of CR1 in a sample corresponds to any particular cancer [sic]." Applicants do not agree.

Preliminarily, claims 69, 70, 75, 76 and 80 have been cancelled, rendering the rejection moot to the extent it refers to these claims. Claims 61, 71, 77-79, 81, 85, 87 and 89 have been amended.

The subject matter of a claim need not be described literally in order for the disclosure to satisfy the description requirement. See, for example, §2163.02 of the MPEP. Rather, claim

limitations must be supported expressly, implicitly, or inherently in the originally filed disclosure. The specification indicates that the sequence set forth as SEQ ID NO:1320 is a CA sequence. The specification at paragraphs [0012], [0013] and [0043] indicates that CA genes are differentially expressed in breast tissue compared to other cells and that breast cancer can be diagnosed using such nucleic acids. Accordingly, the specification provides sufficient support for the pending claims which refer to breast cancer.

Notwithstanding, as discussed above, the claims have been amended to recite that levels of expression product or levels of expression are "altered" in test samples as compared to normal controls. The claims were also revised such that only breast cancer is presently claimed. New claims 91-93 are directed to methods of diagnosing carcinoma based on altered levels of CR1 expression or CR1 expression product. As set forth above, the Office appears to acknowledge that adequate written description exists in the specification for the mis-regulation of CA sequences in carcinoma.

The Office is requested to withdraw the rejection of claims 61, 69, 71, 72, 74-81 and 85-89 under 35 U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. §112, second paragraph

The Office rejected claims 61, 81 and 87 under 35 U.S.C. §112, second paragraph, for allegedly being indefinite. The Office asserts that the metes and bounds of the claims cannot be determined because "carcinoma encompasses various types of malignant neoplasms". Although Applicants do not agree and respectfully assert that one of ordinary skill in the art would readily understand the metes and bounds of the claims given the use of the term "carcinoma", Applicants have amended claims 61, 81 and 87. As revised, claims 61, 81 and 87 no longer recite "carcinoma", thereby rendering the rejection moot.

The Office further alleges that "the claim does not set forth examples from which differences are detected" and that "it is not clear from the claim how evidence is assessed or determined." Claims 61, 81 and 87 have been amended to further clarify the invention and, in particular, to address the Examiner's comments.

In view of the foregoing, Applicants respectfully request the withdrawal of the rejections under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §102

The Office rejected claims 61, 71, 72, 74-76, 81, 85 and 86 under 35 U.S.C. §102 as allegedly being anticipated by Lanza et al. (British Journal of Haematology 77:66-72, 1991). The Office alleged that Lanza “discloses a method of evaluating expression a complement receptor CR1 in patient samples ...”. Applicants do not agree.

Amended independent claims 61, 81 and 87, as well as the claims depending therefrom, recite an active step of diagnosing breast cancer based on changes in the relative level of expression of the CR1 gene or of the relative level of a CR1 expression product in a patient's breast sample. The Lanza reference fails to disclose that breast cancer can be diagnosed based on altered expression of the CR1 gene or based on a change in the level of a CR1 gene product in the patient's breast tissue sample compared to a control sample. Indeed, a review of the Lanza publication failed to locate any reference to CR1 levels in breast samples. Instead, the Lanza publication seeks to correlate CR1 expression with chronic myeloid leukemia (CML). Accordingly, the Lanza publication does not anticipate claims 61, 71, 72, 74-76, 81, 85 and 86. The Office is requested to withdraw the rejection under §102 over the Lanza publication.

The Office rejected claims 61, 71, 72, 74-76, 81, 85 and 86 under 35 U.S.C. §102 as allegedly being anticipated by Guc et al. (Eur. J. Haematol 64(1):3-9, January 2000). The Office alleged that the Guc reference discloses that CR1 expression was lower in acute lymphoblastic leukemia (ALL) and acute lymphomyeloblastic leukemia (AML) than in control groups. Applicants do not agree.

Amended independent claims 61, 81 and 87, as well as the claims depending therefrom, recite an active step of diagnosing breast cancer based on changes in the relative level of expression of the CR1 gene or of the relative level of a CR1 expression product in a patient's breast sample. The Guc reference fails to disclose that breast cancer can be diagnosed based on an change in expression of the CR1 gene or based on a change in the level of a CR1 gene product in the patient's breast tissue sample compared to a control sample. Indeed, a review of the Guc publication failed to locate any reference to CR1 levels in breast samples. Rather, the Guc

publication correlates lower relative CR1 expression with AML and ALL. Accordingly, the Guc reference does not anticipate claims 61, 71, 72, 74-76, 81, 85 and 86.

The Office is requested to withdraw the rejection under §102 over the Guc reference.

Applicants note that neither the Lonza reference nor the Guc reference teach or even suggest the diagnosis of carcinoma as set forth in new claims 91-93. Accordingly, Applicants respectfully assert that new claims 91-93 are also free of the cited art of record.

### Double-Patenting

The Office maintained its provisional rejection of claims 61, 69-72, 74-81, and 85-89 under the judicially created doctrine of double patenting over claims 42, 43, 44, and 49 of copending Application No. 10/573,332, stating that Applicants' request to hold the rejection in abeyance until an indication of allowable subject matter was received was found "unpersuasive since the claimed methods from both applications have not significantly changed substantiating withdrawal of the instant rejection." Applicants note that substantive prosecution of U.S. Ser. No. 10/573,332 has not yet commenced. Upon receipt of a Restriction Requirement or substantive Office Action Applicants may elect subject matter for prosecution different than the subject matter presently claimed.

Applicants renew their request that the rejection be held in abeyance until there is an indication of otherwise allowable subject matter in the present application.

### **CONCLUSION**

It is believed that any pending objections and rejections have been addressed. However, the absence of a reply to a specific rejection, issue, or comment does not signify agreement with or concession of that rejection, issue, or comment. In addition, because the arguments made above may not be exhaustive, there may be reasons for patentability of any or all pending claims (or other claims) that have not been expressed. Finally, nothing in this paper should be construed as an intent to concede any issue with regard to any claim, except as specifically stated in this paper, and the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

Applicant : Malandro, et al.  
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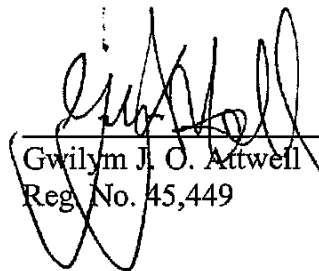
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Applicants submit that claims 61, 71, 72, 74, 77-79, 81, 85-89 and 91-93 are in condition for allowance, which action is requested. Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

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